

Modeling and Dosimetry of Plutonium in Humans

SUMMARY

**Workshop held at the University of Utah
February 22,23, 1999**

Rice-Eccles Olympic Stadium

**Sponsored by the Division of Radiobiology and the Center for Excellence in Nuclear
Technology, Engineering and Research, University of Utah.**

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and the University of Utah**

Workshop objective: To identify scientific issues, critical needs and gaps in our current knowledge to better develop human dosimetric and biokinetic models for exposures to plutonium and other internally incorporated radionuclides.

The morning commenced with Drs. Slaughter, Miller and Khokhryakov presenting the goals of the workshop. It was emphasized that the workshop was designed to address some of the broader issues of plutonium biokinetics, modeling and dosimetry as well as some applications of this information for understanding the consequences of human exposures and the mechanisms of radiation-induced diseases. The summaries here include the presentations and some of the discussion that followed.

Dr. Valentin Khokhryakov (FIB-1). General consideration of the lung clearance models for plutonium.

Dr. Khokhryakov began by discussing some of the issues in ICRP #66 and the need for more biological information to address some of the issues in the ICRP models. He then presented an overview of the FIB-1 model and discussed some of the associated uncertainties with differences in solubility of inhaled particles from different work locations. His evaluations suggest that the solubility characteristics of the particles are more important on the model than is time after exposure for systemic dose calculations. Since most of his autopsy material is from individuals who were exposed much earlier, he is concerned about the assumptions that must be made for the early and intermediate kinetics.

Uncertainties, both procedural and biological, were also discussed as well as the uncertainties associated with the worker exposure histories.

Mr. Ron Kathren (USTUR, Washington State University): Development of new biokinetic models using data from human registries.

Mr. Kathren presented an overview of methods employed at the USTUR for the collection of data on human exposures. He presented some of the historical data from the USTUR on the partitioning between the liver and bone for ^{241}Am . Human data on Pu exposures and the long term retention of Pu in soft tissues, other than the liver, were discussed. The issues of the impact of smoking was raised, and the data on this from both the Russian and U.S. investigators was reviewed. Mr. Kathren emphasized that the USTUR data fits well with the middle solubility group of the Russian data, but not the less or more soluble groups. Thus it appears that the combining of the U.S. and FIB-1 datasets would only be appropriate for this one group of Russian exposures.

Dr. Elena Aladova (FIB-1). Characteristics of aerosol properties in the clearance of plutonium from the lungs.

Dr. Aladova updated the audience on the aerosol, solubility and transportability issues with the works at the Mayak Production Association (MPA). As expected, the amount of residual Pu found in the lungs of the workers depended on the plant and location where they worked. This was due to the differences in the properties of the Pu particles at these work locations, for example, the established differences in the solubility in the Pu dioxide and Pu nitrate particles.

Later in the discussions, 24 investigators agreed to assist in the characterization of the airborne particulates that currently exist at the Mayak. Obtaining this information will enhance our understanding of the biokinetics and dosimetry of the Pu aerosols.

Dr. Ray Guilmette (Lovelace): Lung dosimetry: microdosimetry, biology and toxicity issues.

Dr. Guilmette shared some of the recent liquid emulsion autoradiographs made from lung tissues from exposed MPA workers. The autoradiographs showed the retention of particles (as indicated by 'hotspots') in the tissues. This was apparently most evident in the lymphatic tissues of the lung. Some single alpha tracks were noted in some of the tissues, but were particularly apparent in some of the hyaline cartilage in the bronchial tree. This non-uniformity of dose evoked an interesting discussion on the need for the development of local dose or "cell-based" models for dosimetry. The influence of smoking on the local tissue and cellular distribution of Pu in lung tissues was also discussed.

We note that this presentation was also to be jointly given by Dr. Boecker, but due to a sudden illness, Dr. Boecker was unable to attend. We had asked Dr. Boecker to address the issue of whether some of the large animal inhalation studies that were done in the U.S. could be used to help extrapolate modeling and dosimetry to the human.

Dr. Erich Polig (Karlsruhe, Germany), Dr. Scott C. Miller and Professor Fred Bruenger (University of Utah): A new biokinetic model of plutonium in skeletal tissues.

Dr. Polig lead the discussion on the presentation of a new biokinetic model for plutonium in skeletal tissues and how this model may be used to predict radiation-induced cancers. Incorporated into this model are a number of biological variables that have not been considered in the ICRP models. This new bone model incorporates many important aspects of skeletal biology, such as the

impact of bone remodeling, and appears to be a useful model for predicting the development of tumors. The model is based on data from the D.O.E. beagle studies and has been compared with radium-induced tumors from the dial painter cohort. The discussion focused on the need to incorporate more of the relevant biology into these models to make them more practical and more biologically based.

Dr. V. Vostrotin (FIB-1). Dose assessments for the lung using different models.

This was Dr. Vostrotin's first public presentation and he presented some of his work on dose calculations using various models, including the ICRP-66 and ICRP-30 and a modified model of Pat Durbin. He showed some data fitting retention curves for Pu-oxides.

Dr. K. Suslova (FIB-1). The influence of pathology on the systemic distribution of plutonium.

Dr. Suslova presented data on the relative distribution of Pu between bone and liver in 3 groups of individuals. The first was accidental deaths, the second was those with cancers (except bone), and those with severe liver disease. Those with liver disease had a significantly different partitioning of Pu between the liver and the bone. However, liver pathology did not seem to affect the deposition and retention of Pu in other soft tissues. The retention of Pu, as a % of total Pu, for the various soft tissues was presented.

Dr. Andre Yakovlev (Huntsman Cancer Center, University of Utah). Introduction by Scott Miller: Development of a mathematical model for alpha-particle induced cancers.

Dr. Yakovlev has been developing models of radiation-induced carcinogenesis using data obtained from the U.S.D.O.E.-supported large animal studies. He has worked on this model with Dr. Erich Polig, also a participant in this conference, and this model has become known as the "Yakovlev-Polig model". Dr. Yakovlev presented data concerning the competition between cell killing by alpha particles vs. the promotion of tumor promotion. The model describes and explains, at least in mathematical terms that may have some biological basis, such findings as the inverse dose-rate effect.

Critical issues in lung dosimetry and plutonium biokinetics: Discussion Chairman: Dr. Ray Guilmette (LRRI)

Dr. Guilmette led the discussion the lung dosimetry. He reviewed some of the critical pathways and their biological and dosimetric significance. The discussion also addressed issues such as smoking, the effects of ²¹⁰Po, the compounding effects of exposures to chemical carcinogens, uncertainties in dose estimates for the lungs and the influence of particle size and solubility on lung clearance. From the autoradiographs that were shown in the previous presentation, there was some discussion on the need for further identification of the cells at risk, the necessity to consider non-uniformity of dose, and the biological factors involved in Pu deposition, retention and translocation in the lung. The preliminary autoradiographs from the Mayak workers and the known deposition patterns from previous animal studies suggests that more emphasis should be placed on the lymphatic tissues of the lung. There was also some discussion on the inadequacy of some of the historical

approaches (such as ashing the entire lung) for more modern dosimetry and biology and Pu biokinetics. Dr. Romanov emphasized that in one cohort of lung cancers among 150 individuals, 146 were smokers.

Critical issues in bone dosimetry and plutonium biokinetics. Discussion Chairman: Dr. Erich Polig (Karlsruhe, Germany)

Erich Polig led the discussion on the biological factors that influence the deposition and retention of Pu in skeletal tissues and also the factors that influence the dose to putative cells at risk for cancer induction. Some of the deficiencies of the current ICRP models were reviewed. Important factors that are not considered in many accepted models include the influence of bone remodeling, the predisposition of nuclides for certain bone compartments, the influence of bone remodeling and the non-uniform distribution of tumors from animal studies. There was some discussion of the non-uniformity of dose in skeletal tissues, the resulting effects on cancer induction and the need to further identify the putative cells at risk.

Plutonium localization and biokinetics in bone and some soft tissues. Dr. Scott Miller (University of Utah).

Dr. Miller continued on with the discussion started by Erich Polig and reviewed the techniques used to localize Pu in tissues, specifically neutron-induction methods. Examples were given of the differences in Pu deposition patterns and the biological factors that seem to influence these deposition patterns. Some comparisons were made with Ra and the resultant cancers in the Radium watch dial painters compared with Pu cancers in experimental animals. In addition, conventional and neutron-induced autoradiographs were presented showing the non-uniform distribution of Pu in some soft tissues including the adrenal, testis, and ovary, emphasizing the need for local or cell/tissue-based dosimetry models.

Critical issues in other soft tissue dosimetry and plutonium biokinetics: Chairman. Mr. John Russell (USTUR)

Mr. Russell continued on with the theme of the previous speakers on the non-uniformity of dose in soft tissues. There was some discussion on Pu deposition in the liver and the influence of liver disease, as demonstrated by Dr. Suslova.

Critical issues in the general modeling of plutonium in humans. Discussion Chairman: Dr. Valentin Khokhryakov (FIB-1)

Dr. Khokhryakov emphasized the need to perhaps modify our thinking about local doses in certain tissues based on the non-uniformity of doses and was particularly concerned about Pu deposition patterns at the early and intermediate times after exposures. For this, it was suggested that it might be worthwhile to examine in greater detail and using more modern methods, such as neutron-induction methods, some of the acute exposure cases. The issue of smoking was discussed again by Dr. Romanov. He felt that smoking may be the greatest complicating factor in establishing dose-response effects of internally incorporated Pu.

Specific issues for Direction 2 projects: Development of a consensus on critical issues in the development of new models for human plutonium biokinetics and dosimetry. Discussion Chairman: Dr. Melinda Krahenbuhl.

Dr. Krahenbuhl was charged with summarizing some of the common internal dosimetry issues for the Direction 2 projects. The first major milestone is the delivery of the FIB-1 model and data from this model by April 1, 1999. Our next challenge is to update the existing model, if necessary. Dr. Krahenbuhl presented some data comparing the FIB-1 model against the ICRP model. It was generally agreed that the FIB-1 appears to be particularly good for longer term exposures and agrees with some of the existing models, including the ICRP. However, the fit is not as good for the shorter exposures, perhaps because of the unique characteristics of some of the materials that were produced at the MPA and the resultant differences in systemic transport out of the lung.

Student presentations. Chairman: Dr. Michael Slaughter (University of Utah).

Some students from the College of Engineering presented some of their work that related to nuclear sciences, and dosimetry issues.

Mr. Justin Wilde's presentation showed his study in associating airborne Pu particulate measured at environmental monitoring sites to Pu excretion data from workers at Rocky Flats and Nevada Test Sites.

Mr. Dong-Ok Choe presented his results on internal dose reconstruction from Pu exposure using fission track analysis (FTA) with two neutron energy spectra.

Ms. Stephannie Mecham described her ongoing research in efficiently detecting ultra low levels Pu in a variety of biological and environmental samples.

Ms. Christy Seiger-Webster gave her results on the efficiency and improvements for the anion exchange process used in concentrating of Pu in the FTA technique

Mr. Ross Schmidlein presented his work on the use of Sinc methods for solving ODEs for determining internal dose from Pu exposure. (A new unique mathematical method based on Sinc functions that is computationally efficient.)